

CLAIMS:

1. A method of screening test compounds for probable biological properties comprising the steps of
 - 5 identifying two or more membrane mimetic surfaces each having a unique composition;
 - providing a set of control compounds, each control compound having a known biological property and defining for each control compound an ordered set of numerical values related to its interaction with each respective membrane mimetic surface, whereby said ordered set of numerical values can be represented by the expression $\{C_1, C_2 \dots C_n\}$ wherein n is the number of membrane surfaces;
 - 10 defining an ordered set of numerical values $\{T_1, T_2 \dots T_n\}$ for each test compound related to its interaction with each respective membrane mimetic surface; and
 - 15 comparing the set of numerical values for each test compound with the sets of respective values for said control compounds and identifying the biological properties of those control compounds having ordered sets of numerical values best matching the respective numerical values in the ordered set of values for each test compound.
- 20 X 2. The method of claim 1 wherein the numerical values are defined empirically.
3. The method of claim 1 wherein at least a portion of the numerical values are calculated.
4. The method of claim 1 wherein numerical values relating to the
 - 25 interaction of the compounds with each membrane mimetic surface are determined in a chromatographic system using a mobile phase and a stationary phase comprising said membrane mimetic surface.
5. The method of claim 1 wherein at least one of the membrane mimetic surfaces comprises a head group of a phospholipid compound that occurs naturally in
 - 30 biological membranes.

6. The method of claim 4 wherein each value in the ordered set of numerical values for each respective compound corresponds to the retention time of the compounds in the chromatographic system using a predetermined stationary phase.
7. The method of claim 4 wherein each value in the ordered set of numerical values for each respective compound corresponds to the peak width of the compounds in the chromatographic system using a predetermined stationary phase.
8. The method of claim 1 wherein the membrane mimetic surfaces are selected from liposomes, Langmuir Blodget films, and immobilized artificial membranes.
9. The method of claim 1 wherein the numerical values for T and C for each membrane surface are each normalized against a common reference standard for said membrane surface.
10. The method of claim 1 wherein the best matching control compound are those for which the angle Θ in the formula cosine $\Theta = (T_1C_1 + T_2C_2 + \dots T_nC_n) / (T_1^2 + T_2^2 + \dots T_n^2)^{1/2} (C_1^2 + C_2^2 + \dots C_n^2)^{1/2}$ is less than about 20°.
11. The method of claim 10 wherein the angle Θ is less than about 15°.
12. The method of claim 10 wherein the angle Θ is less than about 10°.
13. The method of claim 4 wherein each membrane mimetic surface is an immobilized artificial membrane.
14. The method of claim 1 wherein at least one of the membrane mimetic surfaces compriseds a mixture of lipid compounds.
15. The method of claim 14 wherein the species and stoichiometric amounts of the respective lipid compounds in the mixture ^{is} corresponds substantially to that occurring in a predetermined biological membrane species.
16. A system for screening test compounds for probable biological properties, said apparatus comprising
 - two or more membrane mimetic surfaces, each having a unique composition,
 - means for quantifying the interaction of the test compounds and control compounds with each of the membrane mimetic surfaces and assigning a numerical value characteristic of said quantified interaction of the compounds for each respective membrane mimetic surface; and

a programmable computer for comparing the numerical values for the test compounds with the numerical values for the control compounds.

17. The test system of claim 16 further including a printer, a display or other means for reporting the control compounds having numerical values best matching those of the test compounds.

18. The test system of claim 16 further comprising a database containing numerical values characteristic of the interaction of selected control compounds for each membrane mimetic surface, at least a portion of said selected control compounds having a predefined biological property.

10 19. The test system of claim 16 wherein the quantifying means is a chromatographic system and the membrane mimetic surfaces are stationary phases for said system.

20. A method of screening test compounds for biological properties comprising

15 selecting two or more membrane mimetic surfaces each having a unique composition,

selecting at least one training set composition comprising one or more control compounds having a common biological property,

20 combining the test compounds with the training set composition to provide a test mixture;

contacting at least a portion of said test mixture with each of the membrane mimetic surfaces to define numerical values characteristic of the interaction of the test compounds and the control compounds with the respective membrane mimetic surfaces; and

25 comparing the numerical values to identify test compounds having numerical values that best match the numerical values for the control compounds.

21. The method of claim 20 wherein the step of contacting the test mixture with the membrane mimetic surfaces is carried out in a chromatographic system wherein each membrane mimetic surface is a stationary phase in said system.

30 22. The method of claim 21 wherein the chromatographic system is a liquid chromatographic system utilizing a mass spectrometric detector.

23. The method of claim 21 wherein the step of comparing the numerical values includes the step of calculating a mean vector for the control compounds in each training set.

24. A training set composition for use in screening test compounds for 5 biological properties *in vitro*, said composition comprising at least two compounds which have a common biological activity, biological function, or clinical efficacy.

25. The training set composition of claim 24 wherein the compounds having common biological activity are present in said mixture in a substantially equimolar ratio.

10 26. The training set composition of claim 24 wherein each of the compounds in the training set exhibits affinity for a multiplicity of membrane mimetic surfaces, and an ellipse plot of the membrane mimetic binding data for the compounds in the training set composition is such that all compounds fall within the 0.95 quartile.

15 27. The training set composition of claim 24, including three or more control compounds.

28. The training set composition of claim 25, including three or more control compounds.

29. The training set composition of claim 26, including three or more control compounds.

20 30. A phospholipid compound of the formula HOOC-W-OPO₂OZ wherein Z is protected glyceryl, 2-(protected amino ethyl), 2-protected carboxyl-2-aminoethyl, 2-protected carboxyl-2-protected amino ethyl or a readily cleavable ester protecting group, and W comprises the lipid residue of a biologically significant amphiphilic compound.

25 31. The compound of claim 30 wherein the biologically significant compound is an amphiphilic compound found in natural biological membranes.

32. The compound of claim 31 wherein the amphiphilic compound is selected from lecithins, lysolecithins, cephalins, sphingomyelin, cardiolipin, glycolipids, gangliosides, and cerebrosides.

30 33. The compound of claim 31 wherein the amphiphilic compound is a phospholipid of the general formula W-OPO₂OB, wherein W is acylglyceryl,

diacylglycerol, or N-acyl 3-O-(protected) sphingosin-1-yl, wherein acyl is C₈-C₂₄ alkanoyl or C₈-C₂₄ alkenoyl.

34. A method for preparing a protected phospholipid of the formula HOOC-W-OPO₂OZ comprising the step of contacting a starting compound of the formula HOOC-W-OPO₂OCH₂CH₂N⁺(CH₃)₃ with phospholipase D(PLD) in the presence of an excess of a protected alcohol of the formula ZOH wherein Z is protected glyceryl, 2-(protected amino)ethyl, 2-protected carboxyl-2-amino ethyl or the residue of an acid protecting group, and W is a lipid residue as of a biologically significant amphiphilic compound with the proviso that W is selected so that the starting compound will serve as a substrate for phospholipase D activity.

35. The method of claim 34 wherein the alcohol is used at about a 3-fold to about a 15-fold stoichiometric excess, and the reaction is carried out in a buffered aqueous organic solvent in the presence of a water soluble calcium salt.

36. A stationary phase for use in a chromatographic system comprising N-(13-carboxyltridecanoyl)-D-erythro-sphingosine covalently bound to a solid support through the 13-carboxyl group.

37. The stationary phase of claim 36 wherein the solid support is silica propylamine.